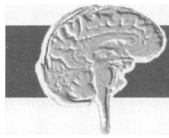

Role of Neurologists in the Pharmaceutical Industry

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Important advances in the field of clinical neuropharmacology have created an increasing demand by the pharmaceutical industry for neurologists. As recently as a decade ago, neurologists were relatively rare in the pharmaceutical industry. I describe the roles played by industrial neurologists and review both the opportunities and risks of this career path.

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The role of neurologists in the pharmaceutical industry has expanded considerably during the past decade. The primary reason for this change is that novel therapeutic agents are being developed that are likely to revolutionize the clinical practice of neurology. These new therapeutic agents, many coming from the biotechnologic advances in molecular biology and genetics, represent neuropharmacologic progress that was impossible to predict a decade ago. A second notable change that has occurred is that most new pharmaceutical neurologists are entering industry directly from academia. In the past, most entry-level pharmaceutical physicians came from private practice. The lure of breakthrough therapeutics is a likely explanation for the change.

The expanding pharmaceutical need for clinician-scientists with neurologic expertise, however, has not been appreciated by most practicing and academic neurologists. Many lack knowledge about the actual roles filled by pharmaceutical physicians—Spilker and Cuatrecasas provide an excellent detailed overview.[1] In this article I review the activities of pharmaceutical neurologists and discuss both the opportunities and risks of this career path.

Role of Neurologists in Pharmaceutical Companies

The question most frequently asked of an industry neurologist by other neurologists is probably, "What exactly do you do all day?" The day-to-day activities can be divided into three major categories: preclinical, clinical, and business-related functions. Although each component is distinct and can vary among corporations in the amount of time spent in each type of activity, industrial neurologists are likely to participate in all three activities to at least some degree.

Preclinical Development Activities

The majority of research personnel in most pharmaceutical companies is engaged in preclinical activities. A neurologist is often part of a "project team" whose goal is to determine the feasibility of a specific therapeutic concept. For example, many pharmaceutical companies are interested in Alzheimer's disease. Preclinical scientists may seek advice from a team's neurologist on whether a certain animal model may be the best available model of Alzheimer's disease or age-related memory impairment. The neurologist needs to keep the preclinical scientists informed of the relative ease or difficulty of possible clinical trials in Alzheimer's disease. The ability to perform cost-effective therapeutic trials with clearly delineated clinical end points may substantially affect management support of the preclinical project.

Ideally the neurologist and preclinical neuroscience group interact closely. In general, less than 10% of preclinical research projects lead to human therapeutic trials. Therefore, the clinician should be actively participating at the earliest stages of a preclinical project. At this early stage, the role of the neurologist is to assess the scientific, clinical, and business logic of the program. Does the scientific hypothesis make sense from a clinical perspective? Is the potential therapeutic product likely to serve an important clinical need? These are key questions that must be answered for every preclinical research project. Neurologists are uniquely able to provide efficient and in-depth answers to these questions.

If a project progresses to the point that clinical trials are considered, the neurologist prepares an outline of the design of the clinical development plan. This "strategic plan" is then presented to the company management committee that oversees all of the drug development plans. Because of the large expense involved with clinical trials,

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the strategic plan needs to be carefully detailed and supported strongly by preclinical data. Pharmaceutical neurologists often rely on clinical consultants at this stage to assist in the development plan. These consultants are usually academic experts in the field of interest. The experience of the consultants and their enthusiasm for the project can have a beneficial effect on the drug development program.

Clinical Development Activities

After the clinical development plan is prepared, it is presented to Food and Drug Administration (FDA) officials for comments at a "pre-IND" [Investigational New Drug] meeting. The neurologist, preclinical scientists, and academic collaborators often attend the meeting. The FDA officials add their unique perspective to the plan, and their comments and suggestions are important to the long-term success of the project. The immediate assessment to be made is whether the Phase I safety study plans are adequate to ensure that all possible biologic or side effects of the drug can be detected, documented, and analyzed.

Once the Phase I safety studies are completed and the data analyzed, then Phase II studies begin. The goal of the Phase II research is to continue to gather safety data while beginning to look for evidence of drug effectiveness. The neurologist also assists with or directs the identification of appropriate clinical investigators who are often, but not exclusively, persons from academia. The neurologist is a key member of the group that designs and implements these critical studies. The neurologist also "monitors" ongoing clinical trials by evaluating all reported side effects and ensuring that the investigators comply strictly with the protocol.

The clinical team within the company working on the trials often includes several clinical research assistants. Clinical research assistants usually have a nursing background and monitor the clinical trials. Statisticians are also important team members because they are primarily responsible for data analysis. The project team also includes persons from the company's regulatory affairs department who maintain contact with the FDA officials throughout the clinical development process.

The next major development decision occurs at the end of the Phase II trials. The assessment of the Phase II data becomes the major determinant of whether drug development should continue. The neurologist plays a key role in the assessment of the Phase II data. If the decision is to continue into Phase III, then an "end of Phase II meeting" is held with FDA officials to review the available data and the specific clinical design plans for the Phase III trials. In general, at least two large-scale Phase III efficacy trials are required by the FDA for a drug to be approved. These trials are both the most critical and expensive part of the entire drug development project. Once again, the neurologist plays a major role in trial design, investigator selection, and trial monitoring.

Business-Related Activities

At each step in the development process, the pharmaceutical neurologist needs to be aware of the influence that purely business-related factors have on the development program. For example, drugs that treat rare and nonfatal diseases may be difficult to develop because of the enormous expenses required to obtain drug approval. At present, it has been estimated that about $200 million is needed to bring a drug to market. This cost must be balanced by the sales potential of the product. Thus, a possibly excellent therapeutic agent for a rare neurologic disease may never get developed because the sales of the drug would not be profitable for the company. The discontinuation of a project for purely business reasons can obviously lead to substantial frustration for advocates of certain drugs.

A pharmaceutical neurologist is also likely to become involved in business-related issues. The neurologist may be asked to comment on the value of specific therapeutic approaches that smaller companies are frequently trying to license to larger companies. On the other hand, a neurologist in a small company may spend a great deal of time and effort trying to convince larger companies to collaborate on a specific project.

Pharmaceutical neurologists often interact extensively with marketing departments. Marketing expertise is needed initially to assess the size of the potential market for a therapeutic candidate. As the drug nears approval, marketing activity increases. Even after a drug is approved by the FDA, the clinician is needed to interact with the marketing group to assess possible Phase IV clinical trials. These Phase IV trials are usually aimed at identifying possible new indications for marketed drugs.

Clearly, most neurologists are poorly prepared for any type of business-related activities involving drug development. Therefore, most companies provide "management training" sessions for their physicians. No academic analogue exists for the type of management training provided, but the training can be extremely important for developing higher level management skills in a clinician.

Opportunities in Industry

Teamwork

Although difficult to quantify, the most important opportunity in industry for a neurologist is the power of teamwork. A neurologist is likely to interact daily with outstanding preclinical scientists, clinical trial experts, regulatory affairs officials, and marketing experts. A unique opportunity exists to interact with intelligent and motivated people with a wide variety of skills. Successful industrial neurologists enjoy this type of interaction, and it is crucial to the success of any given project.

Interaction With Leading Academic Experts

A neurologist is likely to initiate and develop relationships with the academic experts in a given field. For breakthrough therapeutic products, the possible "academic" rewards of successful clinical research can be substantial. The neurologist is usually encouraged to attend and participate in conferences related to specific projects. An

ongoing awareness of the preclinical and clinical advances within any specific therapeutic area is essential to all development projects.

Financial Remuneration

It is commonly assumed that industrial neurologists are compensated well financially. In reality, salaries average about 20% higher than equivalent academic positions. But industrial neurologists may also receive stock options and bonuses that could increase total remuneration considerably. In general, industrial neurologists probably earn more than most academic neurologists but less than many physicians in private practice.

Lifestyle

The most striking difference between the life of an industrial neurologist and other neurologists is the lack of essential clinical responsibilities. In general, no night call is required, although unexpected adverse events may occur at any time during clinical trials. In addition, most corporations allow their clinicians to have a half day per week of clinical time. This usually occurs at a nearby academic center. In general, industrial neurologists probably work on average 40 to 60 hours per week in the office and, in addition, travel about 10% to 25% of the time.

Risks for Neurologists in Industry

Loss of Personal Independence

Although the concept of "teamwork" appeals to many people, it also means that a person may lose much of the sense of "being one's own boss." The perceived value of "independence" is highly subjective, however, and for many persons may not be an issue. On the other hand, industry is unique in that nearly all physicians are essentially under the direction of nonphysicians. Being directed by nonphysicians (usually businesspeople) is often difficult for physicians, given the fact that such people are rare in medical school and house-staff training programs. In addition, marketing departments may have a major influence on clinical projects, which is difficult for a neurologist to appreciate. For example, the "small size of the market" may be cited as a reason to discontinue a research program despite the fact that an effective agent may have been found for a rare medical condition.

Clinical Skills Not Appreciated

A more general problem is that medical training focuses on developing individual skills. These skills may sometimes not receive their appropriate recognition from persons with little medical training or knowledge. Clearly a lack of appreciation of the clinical value of a neurologist can be a major drawback of industrial settings.

Clinical Skills Fade

Clinical skills inevitably decline as a neurologist decreases clinical activities. This change need not be sizable and is certainly not irreversible, but it is unavoidable. Maintaining a half day per week of clinical activity is probably the best way to reduce this risk.

Intellectual Conflict of Interest

The most serious professional risk for a person is the possible intellectual conflicts of interest that may occur. To be successful, the neurologist must believe that a project being developed will be useful. This belief must be constantly balanced by an objective analysis of the data. The desire to obtain "good data" may be based on personal, intellectual, or financial goals. Neurologists in industry, like many academic neurologists, must maintain an objectivity that can be difficult when substantial pressures exist to succeed.

Summary

Neurologists in the pharmaceutical industry are playing an increasingly important role in the development of neuropharmacologic advances. Industry offers the opportunity to perform breakthrough clinical research in a setting that rewards teamwork. The pressure to succeed, however, can be more immediate than in academia and can often lead to unique frustrations. On balance, life in the pharmaceutical industry can be both rewarding and challenging for a neurologist interested in advancing the field of neuropharmacology.

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